Symbiosis
DOI 10.1007/s13199-011-0111-9

BOOK REVIEW

Frank Ryan, Virolution

Collins, London, 2009, 390 pp, price £12.99, [ISBN 978 0 00 731512 3]

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Received: 28 February 2011 / Accepted: 1 March 2011

Virolution by Frank Ryan was published by Collins in 2009 and it includes an introduction and 15 chapters with a glossary of technical terms at the end. Each chapter contains the references used by the author to develop his ideas. The author is a physician known for his previous titles *Tuberculosis: the Greatest Story Never Told* and *Darwin's Blind Spot*. The book starts with a short, friendly introduction where the author confesses his admiration of Jacques Monod though recognizing that his viewpoint was exclusively reductionist and selectionist. Monod believed that mutation was the main source of genetic change. Although he does not consider this argument to be incorrect—but simply one side of the story—Frank Ryan argues that natural selection alone could not have given rise to the evolution of life and its subsequent diversity. Therefore, the core message of *Virolution* is to prove, from an entirely scientific standpoint, that mutation is not the exclusive source of genetic variation.

Readers then move on to the first chapter entitled *An Enigma from the World of Plagues*. Here the author uses the sea slug *Elysia chlorotica* as a case study to show the possible role of viruses in slug's life and death. Referring to recent studies, he argues that viruses not only enable the gene transfer from the nucleus of the alga to the nucleus of the slug but at the same time viruses change their behavior soon after the eggs have been laid, swarming the slug's tissues and organs and causing its death. Referring to the case of hantaviruses, an emerging plague virus that affected in 1993 the Four Corner States of New Mexico, the author shows that viruses are more than parasites. In this context, Ryan had a chance to interview Terry Yates, Professor of Mammals at the University of New Mexico, who demonstrated to him that viruses are more than parasites. Deeply interested in looking into the evolutionary aspects of hantaviruses, Yates introduces Ryan to a new conceptual framework that assumes the co-evolution of a virus in parallel with its host, which he thought to be the case of hantaviruses. This means that both virus and its mammalian host are influencing each other's evolution. The chapter ends with an attempt to develop a definition of viruses that does not depict them merely as a list of chemicals. Rather, it portrays them as a life form that only shows its real nature when it interacts with its natural host.

The following chapter, *Crisis in Darwinism*, starts with an attempt to deconstruct some misleading evolutionary concepts. Referring in particular to the case of the concept "survival of the fittest", generally invoked as the core of Darwin's theory, Ryan shows that this concept was abusively associated with biology by the social philosopher Herbert Spencer, who first proposed it in his book *Principles of Biology*. Although this concept has been the delight of Social Darwinism of the late nineteenth century, the core of Darwin's theory was never the concept of natural selection. Deeply simple in its theoretical formulation, this concept was strongly criticized by the total absence of experimental proof of its main role in the production of new species. Even after the Modern Synthe-

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Published online: 16 March 2011

sis, considered as a key stage in the development and amplification of that vision, the natural selection—a mechanism exclusively based on theory—continues to be regarded as the exclusive creative force. This is something that Ryan considers a misconception given that the two other mechanisms, mutation and Mendelian genetics, are facts that can be proven with all the certainty of modern genetics. Finally, the author refers to diseases that are caused by mutations (e.g. cystic fibrosis and cancer) to illustrate how important it is to fully understand the mechanism of a disease in order to treat it more effectively. However, Ryan argues that mutation is neither the exclusive mechanism of hereditary change in evolution nor the exclusive explanation of the genetic underpinning of disease.

In chapter three, entitled *The Genetic Web of Life*, the author reports an interesting interview with Joshua Lederberg who won the Nobel Prize in 1958 for his discoveries concerning the genetic recombination and the organization of the genetic material of bacteria. During this conversation, Lederberg evoked the concept of symbiosis to state that we should look at living organisms as metabolic nets, capable of reaching out and accepting help, at chemical or even genetic level, from other life forms. Then referring to Jan Sapp's work, the author offers an overview on the history of the concept of symbiosis from Schwendener to Merezhkowskii. Although, according to Darwinian theory, the pattern of evolution is linear (in opposition to symbiosis that involves a reticulate pattern), Frank Ryan argues that symbiosis does not contradict at all Darwin's concept of natural selection. To demonstrate it, he examines two familiar examples of symbiotic partnerships: hummingbirds and cleaner stations. Finally, the author quotes the work of Maynard Smith to show that there is no contradiction between Darwinian and symbiotic evolution. Rather, he says, it's something useful and provides a more profound understanding of the role of symbiotic viruses in human evolution.

The AIDS Dimension is the title of chapter four. Here the author argues that the AIDS pandemic is an evolutionary phenomenon. In other words, this means that retroviruses have a long evolutionary experience, with highly adaptive behavioral patterns. Therefore, he states, pandemic diseases, in particular AIDS, if not exactly predictable, might at least be seen as potentially unsurprising. The author strives to defend his statement interviewing Max Essex, chairman of the Harvard AIDS Institute, about the origin of HIV-1 and HIV-2. The most curious thing here is that Essex's team believes that HIV-1, the main virus of AIDS, was transferred to people from a specific group of chimpanzees. However, the virus grows freely and reproduces in chimpanzee's internal organs and tissues, without evidence of disease. The author ends this chapter with the hypothesis, advanced by Essex, that virus-host symbiogenesis at the most powerful genetic level—the fusion of whole organisms—may have played a constructive role in the evolution of the human genome.

Chapter five, *The Paradox of the Human Genome*, starts with a reference to the DNA breakdown of the human genome, in particular the evidence that the part we normally associate with what makes us human amounts to a mere 1,5% of the whole, while the human endogenous retroviruses, or HERVs, amount to an amazing 9%. The author referred to the case of the newly discovered epidemic virus that was affecting Australian koalas as a good example of an endogenisation process of a virus that has affected the koala population during the last hundred years and which was probably introduced by a rodent. Invoking once again the concept of "aggressive symbiosis", the author intends to show that this concept implies various steps, ranging from the interaction between exogenous virus and host, to plague culling and partnership at the most powerful symbiogenetic level, followed by complete genomic fusion. Finally, the chapter culminates in an extended and interested conversation with the virologist Luis Villarreal, who believes that viruses, and their closely related products, make up at least 43% of the known human genome.

In chapter six, entitled *How Viruses Helped Make Us Human*, the author frames his concept of "aggressive symbiosis" in Darwinian and symbiotic perspective. He does so because, according to him, we cannot possibly interpret the massive viral presence in the human genome if we fail to consider both perspectives. Then, the author uses several examples of HERVs to reach the evolutionary implication of the presence of these endogenous retroviruses in our genome, in particular the role of HERV-R and HERV-K to human foetal development, and therefore to human evolution. This chapter ends with the author presenting the next three chapters, in which he intends to explore the role that this huge viral presence might play in human disease, and in particular in autoimmune diseases and cancer.

Chapter seven, entitled *The Implications for Medicine*, starts with a short explanation about the origin, and in particular the role of, mitochondria in disease. Then, referring to the HERVs, Ryan argues that retroviruses, like mitochondria, began as selfishly evolving parasitic microorganisms. Indeed, that is why we should not be surprised that endogenous retroviruses sometimes cause disease. A long-term holobiontic partnership with its host is followed by a process of endogenisation with the virus entering the host germ lines. Here, virus genes and control sequences are silenced by host defenses through epigenetic mechanisms such as methylation. In fact, this is currently the case with respect to Australian koalas referred in chapter five. The author concludes giving some examples of

diseases related with HERVs such as male infertility and schizophrenia. The case of male infertility is very interesting since it seems that some of the HERVs and their products populating the Y chromosomes serve important physiological functions.

In chapter eight, *The Autoimmune Diseases*, the author provides some common examples of autoimmune diseases like systemic lupus erythematosus, rheumatoid arthritis or Type 1 diabetes. The intention is not to be exhaustive but instead to show commonalities—the failure of the immune system to recognize tissues and cells of the body to which it belongs. Throughout this chapter, the author quotes several works to suggest that human endogenous retroviruses play an important role in these diseases. For example, in the case of multiple sclerosis, scientists have shown there to be a correlation between multiple sclerosis and endogenous retroviruses.

In *Cancer*, the title of chapter nine, the author examines the contribution of viruses, and in particular endogenous viruses, to the understanding of the genetic basis of cancer. Even though there are no firm conclusions about the causative or responsive role that HERV plays in cancer, there is growing evidences that links humane endogenous retroviruses fragments to a variety of cancers. This chapter ends with a brief mention of work done by Spadafora and co-workers which employed anti-reverse transcriptase drugs to reverse the tumour effects in seven different human cancers.

Chapter ten, entitled *The Wider Dimension*, starts with a short historical note on the well-known joint presentation of Darwin and Wallace's papers regarding natural selection at the Linnaean Society on 1st of July, 1858. Then Ryan gives an account of a two-day meeting held in this same historical building, where a broad range of distinguished speakers from different disciplines presented their works and ideas on symbiosis, thus contributing to a modern interpretation of the original synthesis and therefore the mysteries of evolution.

Sex in the Evolutionary Tree is the title of chapter eleven. Here is presented a new conceptual and mechanical understanding of the implications of hybridisation for evolutionary theory. Using wild sunflowers as a model, it was shown that many plant or animal species have evolved through hybridisation not by polyploidy but retaining the same number of chromosomes, a situation known as "homoploid hybridisation". Like symbiogenesis, hybridisation follows a reticulate pattern of evolution bringing together large number of pre-evolved genes from different lineages. In this sense, hybridisation is now considered as a powerful evolutionary force that can even lead to the emergence of new species. Actually, the same pattern was later recognized in animal groups like the case of *Heliconii* or swallowtail butterflies.

Chapter twelve is entitled *Are We Polyploid?* It's a challenging question but Ryan tries to answer it. He starts by referring to the controversial conclusion reached by David Reich that although hominid and chimpanzee lineages have separated more recently than expected, sexual crossing continued between the diverging species. Moreover, there are new genetic findings, e.g. the sequences of the X chromosome region RRM2P4 which indicate an apparent hybridisation between early modern humans and *Homo erectus*. On the other hand, the latest findings for Neanderthal suggest the opposite even though the genomic similarities between early humans and Neanderthal are the same as two unrelated humans. Returning to the original question, the author refers to the case of *HOX* gene clusters (humans have four), as a good argument to think about ancestral polyploidy even though this could have arisen from viral recombination. Hence, for the author, the answer is 'almost certainly yes', which has implications for human evolution and human disease. The chapter concludes with some examples of diseases that in some manner illustrate these implications, in particular the Huntington disease which is caused by a mutation in chromosome 4.

Chapter thirteen, *The Genie that Controls the Genes*. This chapter discusses the role of epigenetic systems, starting with a historical introduction to the concept and ending with a full description about how the epigenetic system actually works. The author pays special attention to DNA methylation given its role in the regulation of the expression of certain genes, though it is not the only epigenetic system (there are others like histone modifications and RNAi). But the underlined argument here is that genes are controlled by what the author calls "genie". This means that, in fact, we are not slaves of our selfish genes as proposed by Dawkins but influenced by environmental factors throughout life. The former notion that one single gene transcribes one single protein, and for this reason we are able to determine everything about a person simply by looking at their genes, is no longer tenable. On the contrary, there is growing evidence that epigenetic inheritance has played an important, non-mutational, role in the evolution of life, just as it continues to play a major role during human embryological development and, in the control of cell division in tissue regeneration and repair throughout our lives.

In *The Coming Epiphany*, the title of chapter fourteen, the author discusses broadly the implications of epigenetics in order to achieve a better understanding of the mechanism of disease. Deficiency in folic acid is a relevant example because the latter is an essential factor in making methionine serve as a donor of the methyl group during DNA methylation. Hence, the lack of folic acid in the mother's diet during pregnancy results in an impaired epigenetic ability in the foetus, which leads

directly to the spinal defect. The author points out other examples but the core message is that various epigenetic mechanisms control the action of genes and those mechanisms can be influenced by environmental changes, something that can be used as an advantage to develop new and more efficient therapeutic approaches. In this sense, the epiphany is coming and we are not able to stop it.

In the final chapter, *At Journey's End*, Ryan resumes some of the arguments presented in previous chapters. Here two important remarks are made. The first one is the idea that the original synthesis needs modernisation. Mutation remains a powerful and mechanically valid force; but there are other important driving forces such as symbiogenesis, hybridogenesis and epigenetic inheritance systems capable of genomic creativity. The second remark is about the consequences of this new way of thinking for Darwin's tree of life. Here the author provides an interesting description of a new tree not as the familiar stout and sturdy oak, but more as the oldest living tree on Earth where symbiotic viruses have a prominent place.

In conclusion, Frank Ryan's book is an important work because it provides a clarification of viruses' role in evolution and it highlights that mutation is not the only driving force for hereditary change. Using several recent and well- studied examples, he shows that symbiogenesis, hybridogenesis and epigenetic inheritance are also powerful mechanisms of genomic creativity. By making a bridge between biology and medicine, Frank Ryan introduces a new perspective on disease and shows that it is possible to develop new tools to fight several plagues of the modern era, such as AIDS and cancer.